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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/813,977	03/31/2004	William S. Dynan	791301-1010	6138

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BRADLEY ARANT ROSE & WHITE, LLP
INTELLECTUAL PROPERTY DEPARTMENT-NWJ
1819 FIFTH AVENUE NORTH
BIRMINGHAM, AL 35203-2104

EXAMINER	
AEDER, SEAN E	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 10/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/813,977	DYNAN ET AL.	
	Examiner	Art Unit	
	Sean E. Aeder, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8,9,11-13,15-17,19,27-32 and 34-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6, 8, 9, 11-13, 15-17, 19, 27-32, and 34-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

The Amendments and Remarks filed 8/9/06 in response to the Office Action of 2/9/06 are acknowledged and have been entered.

Claims 1-19 and 27-39 were pending.

Claims 7, 10, 14, 18, and 33 have been cancelled by Applicant.

Claims 1, 3, 4, 6, 8, 13, 16, 27, 31, 32, 34, 36, and 37 have been amended by Applicant.

Claims 1-6, 8, 9, 11-13, 15-17, 19, 27-32, and 34-39 are currently under examination.

The text of those sections of Title 35 U.S.C. code not included in this Office Action can be found in a prior Office Action.

The following Office Action contains NEW GROUNDS of rejections necessitated by amendments and new grounds of rejections based upon new considerations.

Objections Withdrawn

The objections to the specification are withdrawn in view of amendments.

Rejections Withdrawn

The rejection of claim 4 under 35 U.S.C., second paragraph, is withdrawn in view of amendments.

The rejection of claims 1, 2, 4, 6, 8, 9, 11-13, 15-17, 19, and 27-29 under 35 U.S.C., first paragraph, is withdrawn in view of amendments and arguments.

The rejection of claims 1, 2, 4, 6, 8, 9, 11-13, 15-17, 19 under 35 U.S.C. 102(a) is withdrawn in view of the Affidavit under 37 CRF 1.131 submitted on 8/9/06.

The rejection of claims 1, 2, 4, 6, 8, 9, 11-13, 15-17, 19 under 35 U.S.C. 102(b) is withdrawn in view of amendments.

The rejections of claims 1, 2, 4, 6, 8, 9, 11-13, 15-17, 19 and 27-29 under 35 U.S.C. 103(a) are withdrawn in view of amendments and the Affidavit under 37 CRF 1.131 submitted on 8/9/06.

New Rejections Necessitated by Amendments

New Matter

Claims 1-4 and 37-39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

Claim 1 recites the limitation "said DNA repair modulator not comprising monoclonal antibody 18-2". The limitation "said DNA repair modulator not comprising monoclonal antibody 18-2" is not found in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the invention was filed, had possession of the claimed invention.

Claim 37 recites the limitation "said single chain antibody not comprising monoclonal antibody 18-2". The limitation "said single chain antibody not comprising monoclonal antibody 18-2" is not found in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the invention was filed, had possession of the claimed invention.

New Rejections Based Upon New Considerations

Claim Rejections - 35 USC § 112

Claims 4-6, 8, 9, 11, 12, 15-17, 29-31, and 34-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4-6, 8, 9, 11, 12, 15-17, 29-31, and 34-36 are rejected as vague and indefinite for reciting the terms DNA-PKcs and DNA-PK as the sole means of identifying polypeptides. The use of laboratory designations only to identify a particular molecule renders the claims indefinite because different laboratories may use the same

laboratory designations to define completely distinct molecules. Amending the claims to specifically and uniquely identify DNA-PKcs and DNA-PK by SEQ ID NOs would obviate this rejection.

Claims 5, 6, 8, 9, 11, 12, 30, 31, 35, and 36 are rejected as indefinite for reciting claims drawn to products that bind a region outside of the catalytic domain of DNA-PKcs (see claims 5, 6, 30, and 35). However, it is not clear from the claims or the specification what region of DNA-PKcs consists of said catalytic domain of DNA-PKcs. This renders the claim indefinite because the catalytic domain of DNA-PKcs is not defined by the claim and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Given the above reasons, the metes and bounds of the claims cannot be determined. Amending the claims to specifically and uniquely identify the catalytic domain of DNA-PKcs by SEQ ID NO would obviate this rejection.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-6, 8, 9, 11-13, 15-17, 19, 27-32, and 34-39 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

Claims 1-6, 8, 9, 11-13, 15-17, 19, 27-32, and 34-39 are drawn to DNA repair modulators that specifically bind SEQ ID NO:16 and single chain antibodies that bind outside of the catalytic domain on DNA-PKcs.

The specification discloses examples of DNA repair modulators that specifically bind SEQ ID NO:16 and single chain antibodies that bind outside of the catalytic domain on DNA-PKcs.

The specification prophetically asserts a utility for said DNA repair modulators that specifically bind SEQ ID NO:16 and single chain antibodies that bind outside of the catalytic domain on DNA-PKcs in methods of inducing cell death or apoptosis in cell culture and in vivo (pages 33-34, in particular). The specification further prophetically indicates that using DNA repair modulators that specifically bind SEQ ID NO:16 and single chain antibodies that bind outside of the catalytic domain on DNA-PKcs to induce cell death or apoptosis can be used in treatments of cancers, including, but not limited to surface cancers such as skin cancers, tumors, lung cancer, prostate cancer, colon cancer, testicular cancer, and breast cancer (page 34, in particular). It is noted that the specification lacks working models demonstrating treatment of any disorder with DNA repair modulators that specifically bind SEQ ID NO:16 or single chain antibodies that bind outside of the catalytic domain on DNA-PKcs. As the asserted intended use of the claimed product is drawn to treating almost all cancer, said asserted intended use is not specific.

Following the requirements of the Utility Guidelines, (<http://www.uspto.gov/web/offices/pac/utility/utilityguide.pdf>), "substantial utility" is a

utility that defines "real world use", wherein utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. In the instant case, the asserted "real world" utilities of the claimed DNA repair modulators that specifically bind SEQ ID NO:16 and single chain antibodies that bind outside of the catalytic domain on DNA-PKcs are use of said DNA repair modulators that specifically bind SEQ ID NO:16 and single chain antibodies that bind outside of the catalytic domain on DNA-PKcs in methods of cancer therapy. These asserted "real world" utilities are not supported by the specification or the prior art. The specification and the art lack working models demonstrating treatment of any disorder with DNA repair modulators that specifically bind SEQ ID NO:16 or single chain antibodies that bind outside of the catalytic domain on DNA-PKcs.

Further, therapeutic cancer treatments, in general, are unpredictable, as underscored by Gura (Science, 1997, 278:1041-1042.) who discusses the potential shortcoming of potential anti-cancer agents including extrapolating from in-vitro to in-vivo protocols, the problems of drug testing in knockout mice, and problems associated with cologenic assays. Indeed, since formal screening began in 1955, thousands of drugs have shown activity in either cell or animal models, but only 39 that are used exclusively for chemotherapy, as opposed to supportive care, have won approval from the FDA (page 1041 first column, in particular) wherein the fundamental problem in drug discovery for cancer is that the model systems are not predictive.

Further, those of ordinary skill in the art recognize that treatment in vivo is not predictive. The instant situation is analogous to that of *In re* Brana (34 U.S.P.Q. 2d

1436, 1440 (Fed. Cir. 1995)). A review of *In re Brana* reveals an application that claimed a chemical compound for treating a cancer, wherein the chemical compound was structurally similar to known compounds that have known in vivo use to treat tumors, and more importantly, Applicant provided in vivo data that the claimed compound could treat tumors in mice, hence it was ruled that the claimed compound was enabled for treating tumors. In the instant application, the claims are not drawn to products which have known in vivo ability to give rise to a therapeutic effect. Further, the instant specification provides no in vivo data, particularly demonstrating that the claimed products would predictably give rise to a therapeutic effect in vivo. In view of *In re Brana*, Examiner asserts that successful use of in vivo mouse models of specific disorders enables compositions for specific therapeutic effects in humans and does not require human clinical testing; however, the instant application is claiming products that are intended to provide a therapeutic effect without providing any in vivo data, hence the claimed invention is not enabled. All of this underscores the criticality of providing workable examples which are not disclosed in the specification, particularly in an unpredictable art, such as cancer therapeutics.

Utility must be in readily available form. One of skill in the art would recognize that novel biological molecules, such as the claimed DNA repair modulators that specifically bind SEQ ID NO:16 and single chain antibodies that bind outside of the catalytic domain on DNA-PKcs, lack an established utility and must undergo extensive experimentation to determine an appropriate specific, substantial, and credible utility. It is possible that, after further characterization, the claimed DNA repair modulators that

specifically bind SEQ ID NO:16 and single chain antibodies that bind outside of the catalytic domain on DNA-PKcs might be found to have patentable utility. This further characterization, however, is part of the act of the invention, and until it has been undertaken, Applicant's claimed invention is incomplete.

The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-tumor activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility.

The court held that:

"The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where *specific* benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. . . . a patent is not a hunting license. . . .[i]t is not a reward for the search, but compensation for its successful conclusion."

The instant claims are drawn to DNA repair modulators that specifically bind SEQ ID NO:16 and single chain antibodies that bind outside of the catalytic domain on DNA-PKcs with undetermined biological significance. Until a specific real world utility is attributed to the claimed DNA repair modulators that specifically bind SEQ ID NO:16

and single chain antibodies that bind outside of the catalytic domain on DNA-PKcs, the claimed invention is incomplete. Because the claimed invention is not supported by a specific and substantial utility for the reasons set forth, credibility of any utility cannot be assessed.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 8, 9, 11-13, 15-17, 19, 27-32, and 34-39 are rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know *how to use* the claimed invention.

Summary

No claim is allowed. Claims 1-4 and 37-39 are rejected under 35 U.S.C. 112, first paragraph and claims 1-6, 8, 9, 11-13, 15-17, 19, 27-32, and 34-39 are rejected under 35 U.S.C. 101, but free of the prior art teaching DNA repair modulators that specifically bind SEQ ID NO:16 or a portion thereof and inhibit end joining, wherein said DNA repair modulator does not comprise monoclonal antibody 18-2 or single chain antibodies that bind to DNA-PKcs in a region outside the catalytic domain. The closest prior art for claims 1-6, 8, 9, 11-13, 15-17, 19, 27-32, and 34-39 is Li et al (Nucleic Acids

Research, 2003, 32(20):5848-5857); however, this reference was withdrawn as prior art in view of the Affidavit under 37 CRF 1.131 submitted on 8/9/06.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean E. Aeder, Ph.D. whose telephone number is 571-272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER

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